

CLAIMS

What is claimed is:

1. A method for isolating one or more T cells specific for an antigen of interest, comprising:
 - (a) incubating a sample comprising T cells with said antigen or a derivative thereof;
 - (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2 IFN γ and TNF α IL5 IL-10 and IL-13.
2. The method of claim 1, wherein said antigen is a self-antigen.
3. The method of claim 2, wherein said self-antigen is selected from the group consisting of myelin basic protein, proteolipid protein, myelin oligodendrocyte glycoprotein, collagen type II peptides, heat shock protein, MAGE, PSA, CA125, GAD protein, and tumor associated antigen.
4. The method of claim 1, wherein said antigen is an immunodominant epitope of a self-antigen.
5. The method of claim 4, wherein said immunodominant epitope is selected from the group consisting of residues 83-99 of myelin basic protein and residues 151-170 of myelin basic protein.
6. The method of claim 1, wherein the cells expressing said first and said second markers are selected using antibodies to said first and second markers respectively, or optionally a bi-specific antibody which binds both first and second markers in combination with an antibody which binds said second marker.
7. The method of claim 6, wherein one or more of said antibodies is fluorescently labeled.
8. The method of claim 7, wherein said T cell is selected by fluorescent activated cell sorting.
9. The method of claim 6, wherein said first antibody is conjugated to a magnetic microbead.
10. The method of claim 9, wherein said T cell is selected by magnetic activated cell sorting

11. The method of claim 1, wherein said antigen is incubated with said sample for 1 to 7 days.

12. The method of claim 1, wherein said antigen is incubated with said sample for less than 1 day.

13. The method of claim 12, wherein said antigen is incubated with said sample for less than 16 hours.

14. The method of claim 13, wherein said antigen is incubated with said sample for less than 12 hours.

15. The method of claim 14, wherein said antigen is incubated with said sample for less than 8 hours.

16. The method of claim 15, wherein said antigen is incubated with said sample for less than 4 hours.

17. The method of claim 16, wherein said antigen is incubated with said sample for less than 2 hours.

18. A T cell isolated by the method of claim 1.

19. The method of claim 1 wherein said isolated T cells are T_H1 or T_H2 T cells or a combination thereof.

20. A method for quantifying the number of T cells in a sample, wherein said T cells are specific for one or more antigens of interest, comprising:

- (a) incubating a sample comprising T cells with said antigen or a derivative thereof;
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2 IFN γ and TNF α IL5 IL-10 and IL-13; and
- (c) determining the number of T cells selected by step (b).

21. A method for diagnosing an autoimmune disease in a patient, comprising:

- (a) incubating a sample derived from said patient comprising T cells with one or more autoantigens involved in said disease;
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers

selected from the group consisting of IL-2 IFN γ and TNF α IL5 IL-10 and IL-13.

22. A method for monitoring an autoimmune disease in a patient, comprising:

- (a) incubating a sample derived from said patient comprising T cells with one or more autoantigens;
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2 IFN γ and TNF α IL5 IL-10 and IL-13; and
- (c) determining the number of autoreactive T cells selected by step (a).

23. A method for treating an autoimmune disease in a patient, comprising:

- (a) incubating a sample derived from said patient comprising T cells with one or more autoantigens;
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2 IFN γ and TNF α IL5 IL-10 and IL-13;
- (c) inactivating said selected autoreactive T cells; and
- (d) administering said autoreactive T cells inactivated by step (b) to said patient.

24. A method for producing a composition for the treatment of an autoimmune disease in a patient, comprising:

- (a) incubating a sample derived from said patient comprising T cells with one or more autoantigens;
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2 IFN γ and TNF α IL5 IL-10 and IL-13; and
- (c) inactivating said autoreactive T cells.

25. The method of claims 23 or 24 further comprising expanding the number autoreactive T cells selected in step (b).

26. A composition for the treatment of a patient with an autoimmune disease produced by the method of claim 24 or 25.

27. A method for isolating a nucleic acid encoding a T cell receptor, or a portion thereof, wherein said T cell receptor is specific for an antigen of interest, comprising:

- (a) incubating a sample comprising T cells with said antigen;
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2 IFN γ and TNF α IL5 IL-10 and IL-13; and
- (c) amplifying said nucleic acid encoding a T cell receptor from a T cell isolated by step (b) using at least one first primer specific for the variable region of the T cell receptor gene and a second primer specific for the constant region of the T cell receptor gene.

28. A method for isolating one or more nucleic acids encoding one or more T cell receptors, or a portion thereof, wherein said one or more T cell receptors are specific for one or more antigens of interest, comprising:

- (a) incubating a sample comprising T cells with said one or more antigens;
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2 IFN γ and TNF α IL5 IL-10 and IL-13; and
- (c) amplifying said one or more nucleic acids encoding one or more T cell receptors from T cells isolated by step (b) using at least one first primer specific for the variable region of the T cell receptor gene and a second primer specific for the constant region of the T cell receptor gene.

29. A method for determining the repertoire of nucleic acids encoding one or more T cell receptors, or a portion thereof, in a patient, wherein said one or more T cell receptors are specific for one or more antigens of interest, comprising:

- (a) incubating a sample derived from said patient comprising T cells with said one or more antigens;
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2 IFN γ and TNF α IL5 IL-10 and IL-13;
- (c) amplifying said one or more nucleic acids encoding one or more T cell receptors from T cells isolated by step (b) using at least one first primer specific for the variable region of the T cell receptor gene and a second primer specific for the constant region of the T cell receptor gene; and
- (d) determining the nucleotide sequence of said one or more nucleic acids amplified by step (c).

30. A method for determining the repertoire of nucleic acids encoding one or more T cell receptors, or a portion thereof, in an autoimmune patient, wherein said one or more T cell receptors are specific for one or more autoantigens of interest, comprising:

- (a) incubating a sample derived from said autoimmune patient comprising T cells with said one or more autoantigens;
- (b) selecting one or more T cells that express one or more first markers selected from the group consisting of CD69, CD4, CD25, CD36 and HLADR and one or more second markers selected from the group consisting of IL-2 IFN γ and TNF α IL5 IL-10 and IL-13;
- (c) amplifying said one or more nucleic acids encoding one or more T cell receptors from T cells isolated by step (b) using at least one first primer specific for the variable region of the T cell receptor gene and a second primer specific for the constant region of the T cell receptor gene; and

- (d) determining the nucleotide sequence of said one or more nucleic acids amplified by step (c).